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13. ABSTRACT ***(Maximum 200 Words)***

Since the inception of USAMRU-K in 1969, its activities have centered on the epidemiology, entomology and immunology of the diseases endemic to Kenya, in particular, trypanosomaisis, malaria, leishmaniasis, rift valley fever, and enteric pathogens. Clinical studies to test the safety and efficacy of new drugs and vaccine candidates have also been undertaken primarily at the Kisumu field site. Even though the potential for disease surveillance has been evident, a systematic effort to collect data for the purposes of defining a regional or national action plan was lacking until the inception of GEIS in 2000. During the second year of GEIS work at USAMRU-K, laboratory based diagnostic capability has been improved in the identification of enteric pathogens and determination of antibiotic and antimalarial drug resistance. Efforts to establish a responsive telecommunication network continued with the launching of a USAMRU-K website. This resource would be an essential tool for dissemination of future surveillance data. Additionally, the local personnel trained during this reporting period will greatly improve the chances of establishing a surveillance system for the region.

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NA In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

NA For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

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NA In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

PI - Signature Date

Introduction

US Army Medical Research Unit – Kenya (MRU) is the sole DOD medical research facility in sub-Saharan Africa. Kenya, by virtue of its geography, is especially rich in infectious and emerging diseases. US Army personnel have conducted medical research in Kenya continuously since 1969, for the past 22 years in partnership with the Kenya Medical Research Institute (KEMRI), a semi-autonomous component of the Ministry of Health. Based at its headquarters at Nairobi, MRU conducts significant long-term field operations in western Kenya, near Kisumu, in the high tea plantation area around Kericho, in the Rift Valley, on the coast of the Indian Ocean, and within and around Nairobi itself.

MRU has continued to operate at approximately half strength since 1999, with no dedicated preventive medicine officer arriving until September 2001. The staff shortage has detrimentally affected MRU's ability to perform a cohesive surveillance program. Additionally, this was a year of great staff turnover, which significantly impacted ongoing surveillance projects.

Despite its abbreviated emerging disease program, MRU has been quite successful in those aspects funded by the GEIS program. Much of the progress this year has been in infrastructure and capacity building, in anticipation of new staffs' arrivals in early FY02.

Plasmodium Drug Sensitivity

Staff: Captain Jon Davis, BS MRU, Clinical Laboratory Officer; Bernards Ogutu, MD KEMRI/MRU; Rachel Achilla, MSC, Research Officer, MRU; Pamela Liyala.

Background: Chloroquine resistant falciparum malaria has become a significant factor in case management. Clinical evidence has been mounting that there exists in sub-Saharan Africa extensive resistance to chloroquine, pyrimethimene-sulfadoxone, quinine, and many other mainstay antimalarial agents. This is not surprising, given the high transmission rates through much of sub-Saharan Africa, the low per capita incomes, the inadequate health services, and the easy availability of antimalarials on the open market. In FY00, MRU stood up the first fully operational in vitro testing facility for plasmodium drug sensitivity in equatorial Africa. Prior to establishing this in vitro testing facility, there had been no attempt to objectively and systematically determine and plot resistance. Although Africa has areas with some of the highest transmission rates in the world, it has many areas where transmission is hypo- or mesoendemic and where lower drug pressure may have left P facliparum susceptible to chloroquine and Fansidar.

Progress and Accomplishments: In FY01, the most important accomplishment has been the technology transfer to allow a pLDH ELISA based system to be used at MRU.

Pamela Liyala traveled to the United States for a period of 6 weeks to train on the use of this technology.

Continuation of projects from FY00 gave the lab some additional experience in using these techniques. Samples archived from previous studies in Somalia (1991), Kisumu (1995), Kenyatta National Hospital (1996), and Magadi/Entesopia (1998) underwent in vitro testing for antimalarial sensitivity. Receipt of samples from AMREF has not been forthcoming. In the future, other collaborative centers will be sought.

The progress of this project has been slowed somewhat by the matriculation of both the KEMRI supervisor, Maurice Adoyo-Adoyo, and the chief technologist, Uzma Alam, into further graduate training programs.

Coincident with systematic culture and in vitro testing, we also amplify the DNA of parasites to check for Multidrug resistance genes. Should the occurrence of mDR genes match that of in vitro resistance, the PCR technique would be a rapid and economical alternative. Currently, primers for both DHFR (folate resistant) and DHPS (anti-folate resistant) genes are being tested.

Hemorrhagic Virus Surveillance and Discovery

Staff: Lee Dunster, PhD, WHO Virus Reference Centre, KEMRI, Head; Manuella Dunster, MS, WHO Virus Reference Centre, KEMRI, Deputy Head; CPT Jon Davis, BS, MRU, Clinical Laboratory Officer; WHO, CDC, Ministry of Health.

Background: Equatorial Africa has been the source of the most devastating and refractory emergent viruses in the world. Many of these, from several different groups, are characterized by profound hemorrhaging and often are either vector-borne or have feral reservoirs. The importance of non-human components in the cycle is that transmission is closely tied to terrain and epidemics to changes in land use or climate. Although frequently deadly during epidemics, their rarity in the West has prevented vaccine programs from developing. However, the pace of new virus discovery (HIV, Ebola, Marburg...being recognized in only the last 25 years or less) indicates that many unknown viruses exist with epidemic potential.

GEIS has attempted to exploit the newly rejuvenated Yellow Fever Network for Kenya, operated by the WHO Reference Centre for Hemorrhagic Viruses as a passive, sentinel system for the detection of virus outbreaks. Additionally, GEIS attempted to use these sites for active collection of serum of inpatients with fevers of unknown origin, to begin to track the epidemiology of fever diseases. The network consists of 24 governmental and non-governmental clinics and hospitals distributed widely across Kenya, excluding the politically unstable northeast. All of these clinics have received training and have agreed to follow a strict case identification paradigm.

Progress and Accomplishments: Without field workers dedicated to this project or a full-time epidemiologist assigned to GEIS, it has been difficult to maintain the activity of the Yellow Fever Network. Reasons for this remain unclear, but could include waning interest among participating clinics, change in personnel in participating clinics, lack of funds to obtain blood, difficulty in arranging transportation of the samples, and other unknown barriers. Another barrier has been the inability to obtain primers and RNA for Lassa, Ebola, and Marburg. These were expected in FY01, but are now not expected until FY02.

Enterics Drug Sensitivity and Pathogen Discovery

Staff: Willy Sang, MS, Centre for Microbiological Research, KEMRI; CPT Jon Davis, BS, MRU; Michael Auko, MRU; Valarie Oundo, MRU; Denis Odera, KEMRI; African Medical and Research Foundation, Nairobi; CDC, Atlanta; Uniformed Services University of Health Sciences

Background: Little is known about prevalence or patterns of drug resistance of enteric pathogens in Africa, despite dysentery being one of the top three causes of infant and child mortality. In recent years, our surveillance efforts have been in conjunction with AMREF, which has a potentially wide network of clinics. Our GEIS-supported laboratory has discovered the first confirmed cases of E Coli O157:H7 and S dysenteriae Type-12 in Africa. Additionally, our lab determined that resistance to 3 or more antibiotics was found in 76% OF 270 Shigella specimens from Entasopia. 67% of the enterohemorrhagic E coli specimens from the same site were found to be multiply drug resistant.

Progress and Accomplishments: AMREF has not been forthcoming with parasitology or specimens. Our association with them was terminated this past year. During FY01, a study of diarrhea etiology and antibiotic susceptibility was completed in Marhare Clinic, in a Nairobi slum. 424 samples were processed between Feb 2000 and Oct 2001. The isolates included 29% *Shigella*, 19% pathogenic *E. coli*, 17% *Campylobacter*, 3% *Salmonella*. Antibiotic sensitivity analysis showed high rates of resistance among enteropathogenic E Coli and Shigella species to multiple antibiotics, including tetracycline, ampicillin, chloramphenicol, erythromycin, and sulfamethoxazole.

Urban Malaria

Staff: Ray Dunton, PhD, MRU; Amy Korman, PhD, MRU.

Background: The increase of urbanization throughout Sub-Saharan Africa and accompanying population mobility is introducing malaria into areas previously considered malaria-free. A 1998 clinical study in Nairobi, Kenya suggested that malaria transmission might occur in certain parts of the city. In 2000, we began routine surveillance for anopheline mosquitoes in Kibera, a shantytown district of Nairobi, based on data from the clinical study.

Progress and Accomplishments: Surveillance continued during 2001. Short rains began in October and November and two anophelines were collected between December 2000 and February 2001. Both specimens were identified by PCR as *Anopheles arabiensis*. Collections continued after the rains began in April 2001. Thirty-six specimens were collected during the Dec00-Oct01 collection period. Two specimens were identified as *An. gambiae*; the rest were *An. arabiensis*. Both of these species are efficient vectors of malaria in East Africa. We identified small polluted streams as dry season breeding sites. No infective mosquitoes (CS-ELISA) were collected. Collaboration with the African Medical Research Foundation (AMREF) Kibera clinic will allow us to expand our surveillance during the rainy season of Nov-Dec 2001 to focus on factors associated with homes of individuals suspected of receiving local malaria infections.

This project supports a crew of 10 full-time collectors, two full-time employees of the ELISA lab, and one PCR technician.

Dengue Vector Surveillance

Staff: Ray Dunton, PhD, MRU; Amy Korman, PhD, MRU.

Background: *Aedes aegypti* is the primary potential dengue vector on the coast of Kenya although other *Aedes* species are present.

Progress and Accomplishments: During 12 months of indoor day resting collections in Kilifi, the paucity of collected adults indicates that *Ae. aegypti* is not a household mosquito, unlike *Ae. aegypti* in Asia. Along the coast of Kenya, it does not rest indoors nor does it oviposit indoors. This project complements other *Aedes* research on the coast. We have found that adult *Ae. aegypti* are not attracted to traps positioned in houses. Vector surveillance is continuing to determine arbovirus transmission ecology in East Africa. This project supported two full-time collectors and five collectors at 0.5-0.75 percent effort.

Training

GEIS funded much education and training of Kenyan employees during FY01. Mr. Maurice Adoyo-Adoyo studied for an MSc degree at the London School of Hygiene and Tropical Medicine from August 2000 to September 2001. He submitted a thesis entitled "The use of pfmdr1/pfcrt as molecular markers in estimating the prevalence of chloroquine resistance in Kenya, Gabon and Sudan" as partial fulfillment of his degree requirements. He will be awarded a diploma in February 2002. Mr Adoyo Adoyo will now play a leadership role in KEMRI's emerging diseases effort. Ms Alam is a PhD candidate at the Johns Hopkins School of Hygiene and Tropical Medicine, Baltimore, MD. Upon completion, she will join the KEMRI staff as a Principal investigator in the emerging diseases surveillance program. Ms. Pamela Liyala received training in malaria drug sensitivity testing at the Division of Experimental Therapeutics, Walter Reed Army Institute of Research, Silver Spring, MD. This training was essential in establishing the first drug sensitivity testing laboratory for plasmodial parasites in the East African region.

Communications and Infrastructure Support

Staff: Alexander Sio Onyango, BSEng, MRU, Systems Manager; Caroline Tungwony, MRU, Webmaster.

Background: Kenya has a poor and deteriorating infrastructure. Dependable and rapid communications are essential for surveillance and for epidemic response. Installation of a direct satellite link by Very Small Aperture Terminal (VSAT) antenna at Nairobi in March, 2000 provided much more reliable communications for MRU and its Nairobi collaborators at CDC, JICA, WHO Virus Reference Center, and the Wellcome Foundation. The KEMRI system was linked to and technically supported by the MIMCOM net, a joint effort of the Fogarty Foundation and the National Library of Medicine.

Progress and Accomplishments: GEIS continued to support the VSAT and MIMCOM systems, allowing for very reliable internet connection and communication among MRU staff, KEMRI, and other collaborators. The largest communication accomplishment in FY01, however, was the launch of the USAMRU-K website, found at http://www.usamrukenya.org. This exciting new tool for information dissemination is in its infancy, but is expected to become a primary means of data and information dissemination.

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